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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
PETERSEN, CLARK D	
ART UNIT	**PAPER NUMBER**
1657	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/655,878	SOMBERG ET AL.	
	Examiner	Art Unit	
	Clark D. Petersen	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,14-18,22 and 24-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-11,14-18,22 and 24-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This action is in response to the amendment, filed 8 May 2007, in which claims 13, 19-21, and 23 were canceled and claims 1-3, 14, and 22 were amended.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

All objections and rejections not repeated in the instant Action have been withdrawn due to Applicant's response to the previous Action.

Remarks – Double Patenting

Examiner acknowledges receipt by the Office of a terminal disclaimer regarding overlapping claims between the instant application and patent 7,083,911. Based upon submittal of this form, the rejection in the Office Action mailed 8 February 2007 is withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 14-18, 22, and 24-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an ATP-consuming

transferase such as a kinase, does not reasonably provide enablement for all transferase enzymes.

This is a new rejection.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. Claims 1-3 all recite that the instantly claimed method is practiceable with any transferase. However determination of transferase activity is dependent upon measuring the amount of ATP consumed; therefore it is impossible using the present invention to determine the activity of transferases which do not directly depend on ATP consumption. Claims 14-18, 22, and 24-26 are rejected because they depend from claims 1-3.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-12, 14-18, 22, and 24-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-3 refer to a "chemostable luciferase". The specification only defines "chemostable luciferase" vaguely in stating "preferred luciferases of the invention have enhanced chemostability in the presence of transferase quenching agents..." (p. 22, lines 12-13).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8, 14-17, 22 and 24-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Crouch et al. (2001) in view of Simpson et al (J Biolum and Chemilum, 1991).

This rejection was previously presented in the Office Action mailed 8 February 2007, and is slightly modified as necessitated by Applicant's amendment.

Crouch et al teach a method of detecting kinase activity. This method comprises combining a kinase, ATP and substrate for the kinase and allowing an enzymatic reaction to occur. They teach that the enzymatic reaction solution also comprises a luciferase enzyme and a luciferin, and that by measuring the bioluminescence of the solution, one can determine how much ATP was consumed by the kinase reaction, and therefore the activity of the kinase (see Abstract; see claims 43 and 44, as examples). Crouch et al also teach that the kinase reaction can be allowed to proceed for a certain amount of time before the addition of the luciferase and luciferin (see p. 3 para [0061], for example). Crouch et al teach that this method is useful for identifying compounds which can modulate kinase activity (see p. 3, para [0046], for example). Crouch et al also teach that this method is useful for high-throughput screening of compounds that

might influence kinase activity (see p.4-5, para [0085] for example). Crouch et al also teach working examples of specific kinases for which this method is applicable. For example MAPK can be tested (see p. 6, Example 2, paras. [0106]-[0110], for example) for its ability to phosphorylate its substrate Myelin Basic Protein, and also MEK can be studied for its ability to phosphorylate its substrate MAPK(see p. 7, Example 7, paras. [0115]-[0116], for example). Crouch et al also teach that, in a method of studying a compound's influence on a kinase's activity, the effect can be either an inhibition or an activation of the kinase (see p. 3, paras [0053]-[0058], for example).

Crouch et al do not teach the addition of kinase reaction stopping agents that comprise detergents.

However Simpson et al studied the effects of various types of detergents on the biochemical kinetics of the luciferase/luciferin reaction. They studied anionic, nonionic, and cationic detergent types and measured stability of the luciferase enzyme, rate of reaction, and whether detergents increased or decreased the luminescent signal detected from the reaction (see Materials and Methods; see Table 1, p. 100, as examples).

Specifically they test the effects of sodium dodecyl sulfate (SDS), dodecyltrimethylammonium bromide, and cetyltrimethylammonium bromide on luciferase activity, and beneficially report that SDS does not interfere with luciferase activity, and dodecyltrimethylammonium bromide, and cetyltrimethylammonium bromide temporarily increase the stimulation of luciferase (see Table 1, p. 100).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use a secondary solution comprising luciferin, luciferase and a detergent in a method of detecting transferase activity taught by Crouch et al, because Simpson et al teach that it is possible to add a detergent to a solution containing components of a luciferase/luciferin ATP assay system, and detect measurable light signals. One would have been motivated to do so because Simpson et al point out that the possibility exists – and they subsequently demonstrate – that detergents have an ability to stimulate luciferase activity and thus could be used to reduce assay costs or to increase assay sensitivity (see p. 98, col. 1, for example).

Based upon the teachings of the cited references and the level of skill of one of ordinary skill in the art, there would have been a reasonable expectation of success in practicing the claimed invention.

Claims 1-10, 14-17, 22 and 24-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Crouch et al. (2001) in view of Simpson et al (J Biolum and Chemilum, 1991) and further in view of Briggs et al (Biochem, 2000).

This is a new rejection necessitated by Applicants' amendment.

The teachings of Crouch et al and Simpson et al are discussed above and applied as before.

Neither reference expressly teaches Src, Lck, Fyn, or Lyn is the kinase studied.

Briggs et al teach that the Src family of proteins are tyrosine kinases. They expressly mention Src, Lck, Fyn and Lyn as being members of this family, and having

tyrosine kinase activity (see Abstract; p. 489; see Introduction, pp. 489-490, as examples).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use Src family tyrosine kinases in a method of studying transferase activity with a luciferin/luciferase system taught by Crouch et al and Simpson et al, because they teach that their system is useful with kinases generally, and Briggs et al teach that Src family proteins, specifically Src, Lck, Fyn and Lyn, are in fact kinases. One would have been motivated to do so because Briggs et al teach that Src family kinases are important in disease progression; for example they may play a role in AIDS progression (see Abstract, p. 489, for example) in a way that is still not understood.

Based upon the teachings of the cited references and the level of skill of one of ordinary skill in the art, there would have been a reasonable expectation of success in practicing the claimed invention.

Claims 1-8, 11, 14-17, 22, and 24-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Crouch et al. (2001) in view of Simpson et al (J Biolum and Chemilum, 1991) and further in view of Lev (EMBO J, 1991).

This is a new rejection necessitated by Applicants' amendment.

The teachings of Crouch et al and Simpson et al are discussed above and applied as before.

Neither reference expressly teaches EGFR, PDGFR or c-KIT is the kinase studied.

Lev et al teach that EGFR, PDGFR, and c-KIT are all growth factor receptors, specifically receptor tyrosine kinases, and that all have kinase activity as an essential aspect of their biology (see Abstract, p. 647; see Discussion, pp. 652-3, as examples).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use growth factor receptor family tyrosine kinases in a method of studying transferase activity with a luciferin/luciferase system taught by Crouch et al and Simpson et al, because they teach that their system is useful with kinases generally, and Lev et al teach that growth factor receptor family proteins, specifically PDGFR, EGFR and c-KIT are in fact kinases. One would have been motivated to do so because Lev et al teach that growth factor receptor kinases are protooncogenes that stimulate mitogenesis (see Introduction, p. 647, for example), and are therefore of interest in cancer research.

Based upon the teachings of the cited references and the level of skill of one of ordinary skill in the art, there would have been a reasonable expectation of success in practicing the claimed invention.

Response to arguments - 35 USC § 103

Applicants traverse the rejection of claims 1-8 and 19-26 in the Office Action mailed 8 February 2007 under 35 U.S.C. 103(a) as being unpatentable over Crouch et al. (2001).

Based on Applicants' amendments to the claims, this rejection is withdrawn.

Applicants traverse the rejection of claims 1-8, 13-17 and 19-26 in the Office Action mailed 8 February 2007 under 35 U.S.C. 103(a) as being unpatentable over Crouch et al. (2001) in view of Simpson et al (J Biolum and Chemilum, 1991).

Applicants argue that there is no motivation to combine the teachings of Crouch et al with the teachings of Simpson.

Applicants' argument has been fully considered but is not deemed to be persuasive. Crouch teaches that it is desirable to add a test kinase with a substrate and allow the reaction to proceed for a certain amount of time before adding substrate and luciferase. One would be motivated to combine the luciferase with a detergent because Simpson et al teach that adding a detergent increases the signal generated by luciferase in the presence of ATP. They expressly state that adding a detergent can decrease reagent costs and improve assay sensitivity. Whether the detergent quenches the kinase or not is inherent to the assay. One would be motivated to add detergent regardless of whether one called it a "transferase quenching agent" or a "luciferase enhancing agent". One would in both cases be motivated to perform the steps claimed in the instant application.

Applicants traverse the rejection of claims 1-10, 13-17, and 19-26 in the Office Action mailed 8 February 2007 under 35 U.S.C. 103(a) as being unpatentable over Crouch et al. (2001) in view of Briggs et al.

Applicants argue that Briggs et al add nothing to remedy the deficiencies of Crouch et al. As discussed above the combined teachings of Crouch et al and Simpson et al render obvious the instant set of claims; the teachings of Briggs et al merely extend the method to the specific kinases of instant claim 10.

Applicants traverse the rejection of claims 1-8, 13-17 and 19-26 in the Office Action mailed 8 February 2007 under 35 U.S.C. 103(a) as being unpatentable over Crouch et al. (2001) in view of Simpson et al (J Biolum and Chemilum, 1991).

Applicants argue that Lev et al add nothing to remedy the deficiencies of Crouch et al. As discussed above the combined teachings of Crouch et al and Simpson et al render obvious the instant set of claims; the teachings of Lev et al merely extend the method to the specific kinases of instant claim 11.

Conclusion

No claims are allowed.

Because examiner has presented new grounds of rejection in this Office Action, it is NOT FINAL.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Clark D. Petersen whose telephone number is (571)272-5358. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on (571)272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CDP
7/19/2007

Jon Weber
Supervisory Patent Examiner